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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,317	09/26/2005	Atsushi Miyawaki	P26359	5682

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
10/05/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/516,317

Applicant(s)

MIYAWAKI ET AL.

Examiner

Rita Mitra

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 May 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 1-9, 16 and 17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-15 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 December 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>3/17/2005, 7/25/2006</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restriction

Applicants' response to the Restriction Requirement mailed April 24, 2007, filed May 22, 2007 is acknowledged. Applicants have elected with traverse of Group II, Claims 10-15 and 18. The traversal is on the ground(s) that a claimed DNA molecule encoding protein X, shares a corresponding technical feature with the protein X according to the PCT International Search and Examination Guidelines, Part III, Chapter 10, example 39.

In response to Applicant's traversal, the Examiner finds arguments not persuasive because as explained in the previous Office action, the technical feature is taught by the prior art as disclosed in the reference of Miyawaki et al. (Midoriishi, March 2002, No. 13, pages 1-4). The reference teaches cloning of DNA that encodes a fluorescent protein from *Cnidaria* including coral and sea anemone. Because *Cnidopus japonicus* was a known species of sea anemone at the time this application was filed, persons skilled in the art could easily select *Cnidopus japonicus* as the *Cnidaria* in the reference and clone the DNA that encodes the chromoprotein from *Cnidopus japonicus*, which corresponds to the invention of Group I, in the recitation of "a chromoprotein having either one of the following amino acid sequences: (a) the amino acid sequence shown in SEQ ID NO: 1; and (b) an amino acid sequence comprising a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1, and having light-absorbing properties," and thus, the shared technical feature of the groups I (a chromoprotein) and II (a DNA encoding a chromoprotein) is not a "special technical feature" even if the chromoprotein is encoded by the DNA. Therefore,

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unity of invention between the groups does not exist. The requirement is still deemed proper.

Status of the Claims

Claims 1-9 and 16-18 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Therefore claims 10-15 and 18 (in part) are currently under consideration.

Objections to the Oath or Declaration

A new oath or declaration is required because of following informalities. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: the title of the application is not "Chromoprotein."

Specification Objections

The disclosure is objected to because of the following informalities:

- 1) The continuity data has not been entered at page 1, line 1 of the specification.
- 2) The abstract of the invention is objected to for using the word "novel." It should be noted that novelty is a determination of the office not an assertion by Applicants.

A correction is required.

Claim Objections

Claims 10 and 18 are objected to because of the following informalities:

Claims 10 and 18 are objected to because they depend from a non-elected claim (in part), and also for containing non-elected subject matter.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10-13 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claimed product, as written, does not sufficiently distinguish over the naturally occurring product in living organisms, i.e., DNA of *Cnidopus japonicus*. In the absence of "the hand of man", the naturally occurring processes are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980) and M.P.E.P. 2105. "A DNA" is a non-statutory subject matter. A correction to read "An isolated and/or purified DNA" would overcome this rejection.

Claim Rejections - 35 U.S.C. § 112.

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The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-15 and 18 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to a genus of DNAs of either one of followings: (a) DNA encoding the amino acid sequence shown in SEQ ID NO: 1 and (b) any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1, and having light-absorbing properties.

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus [compositions or methods], it must be clear that: (1) the identifying characteristics of the claimed [compositions or methods] have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

The specification discloses an example of an isolated nucleic acid sequence comprising SEQ ID NO: 2 which encodes a chromoprotein from *Cnidopus japonicus*. However, this is an inadequate written description for a genus of DNAs of either one of followings: (a) DNA

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encoding the amino acid sequence shown in SEQ ID NO: 1 and (b) any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1, and having light-absorbing properties.

The specification does not provide a disclosure of any particular structure to function/activity relationship in any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1. The specification also lacks description with respect to what function, if any, is required for any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1. Though Examples 4 and 5 describes the mutants claimed in claim 13, however no function has been demonstrated.

In addition based on open language "comprising", the claimed protein can have sequences added to the N-terminal or C-terminal end and any polypeptide or peptide, having an undefined structure. Therefore, there is lack of written description as to what are those variants, which have some activity related to the activity of the protein of SEQ ID NO: 1 protein.

Given the lack of additional representatives of a genus of DNAs of either one of followings: (a) DNA encoding the amino acid sequence shown in SEQ ID NO: 1 and (b) any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1, and having light-absorbing properties as encompassed by the claim, Applicants have failed to

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sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 10-15 and 18 are rejected under 35 U.S.C. 11-2, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for an isolated nucleic acid sequence comprising SEQ ID NO: 2 which encodes a chromoprotein from *Cnidopus japonicus*, does not reasonably provide enablement for any DNA of either one of followings: (a) DNA encoding the amino acid sequence shown in SEQ ID NO: 1 and (b) any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1, and having light- absorbing properties. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The Court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key Word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered

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in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

Claims 10-15 and 18 are so broad as to encompass any DNA of either one of followings: (a) DNA encoding the amino acid sequence shown in SEQ ID NO: 1 and (b) any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1, and having light-absorbing properties.

The claims rejected under this section of U.S.C. 112, first paragraph, do not place any structural limits on the "any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1." Since the nucleic acids encoding a polypeptide determines its structural and functional properties, predictability of which nucleic acid sequence can be used while obtaining the desired function in the encoded protein requires a knowledge of and guidance with regard to which nucleic acids and amino acids of the polypeptide's sequence, if any, are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the nucleic acid sequence and its encoded polypeptide's structure relates to its desired function. In addition, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of different DNA

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sequences and encoded polypeptides. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1 because the specification does not establish: (A) a rational and predictable scheme for modifying any nucleic acid residue with an expectation of obtaining the desired biological function in the encoded polypeptide; and (B) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Because of this lack of guidance, and the fact that the relationship between the polynucleotide sequence and the encoded proteins' activity/function is not well understood and unpredictable (e.g., see Ngo et al. in "The Protein Folding Problem and Tertiary Structure Prediction," 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to make and use the claimed invention.

The scope of the claims must bear a reasonable correlation with the scope of enablement

(In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1 while having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10-12, 14, 15 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Lukyanov et al. (US 6969597). Lukyanov et al. teach nucleic acids isolated from *Anemonia sulcata*, wherein said nucleic acid encodes non-aggregating chromo/fluoroproteins and mutants thereof (col. 1 line 65). Lukyanov et al. teach a polynucleotide of SEQ ID NO: 9, which encodes a polypeptide which has 62.5%% sequence identity to SEQ ID NO: 1 of the instant application (see SEQ ID NO: 1 sequence alignment Result 1, database: Issued_Patents_NA) and wherein SEQ ID NO: 9 of Lukyanov et al. has a 48.2% sequence identity to instant SEQ ID NO: 2 (col. 37), (see SEQ ID NO: 2 sequence alignment Result 1, database: Issued_Patents_NA) thus anticipating claims 10-12. Lukyanov et al. also teach a DNA sequence (see in the attached sequence alignment) encoding an amino acid sequence comprising a deletion, substitution and/or addition of several amino acids with respect to SEQ ID NO: 1, wherein said amino acid sequence

is a fluorescent protein, anticipating claims 11 and 12. In the Experimental section, Lukyanov et al. teach nucleic acids encoding non-aggregating chromo/fluoroproteins and mutants were cloned into pQE30 vector and transformed into *E. coli* to express fluorescent proteins (col. 31 lines 30-35), (claims 14 and 15). The reference also teaches kits comprising nucleic acid and vectors that can be engineered to express the fluoroproteins (col. 3 line 40), thus anticipating claim 18.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10-12, 14, 15 and 18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-7 and 10 of copending Application No. 10/516,314. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a DNA encoding an amino acid sequence, which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1, and has light-absorbing properties and both claims are supported by almost identical specifications.

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. § 3.73(b).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowable.

Inquiries

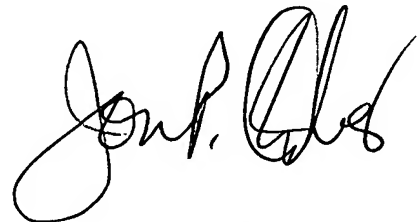
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita Mitra whose telephone number is 571-272-0954. The examiner can normally be reached on M-F, 10:00-7:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Rita Mitra, Ph.D.

September 19, 2007



Jon Weber
Supervisory Patent Examiner